

CLAIMS

1. A pseudo-thermosetting neutralized chitosan composition, which comprises 0.1 to 2.0 wt/v %, based on the total composition, of a homogeneously reacetylated chitosan derived from a chitosan having a deacetylation degree of 80 – 90 %, having a molecular weight of not smaller than 200 kDa and a deacetylation degree of 30 – 60 %, neutralized with an hydroxylated base, wherein said composition forms a phosphate-free transparent hydrogel at a temperature higher than 5°C.

10 2. The pseudo-thermosetting neutralized chitosan composition according to claim 1, comprising 0.5 to 1 wt/v %, based on the total composition, of said homogeneously reacetylated chitosan.

15 3. The pseudo-thermosetting neutralized chitosan composition according to claim 1 or 2, wherein the deacetylation degree of said homogeneously reacetylated chitosan is 45 to 55 %.

20 4. The pseudo-thermosetting neutralized chitosan composition according to anyone of claims 1 to 3, wherein the molecular weight of said homogeneously reacetylated chitosan is not smaller than 600 kDa.

25 5. The pseudo-thermosetting neutralized chitosan composition according to anyone of claims 1 to 4, further comprising a diol having a distance of at least 4.7 Å between its hydroxyl groups.

6. The pseudo-thermosetting neutralized chitosan composition according to claim 5, wherein said diol is 1,3-propanediol.

30 7. A process for producing a homogeneously reacetylated chitosan having a molecular weight of not smaller than 200 kDa and a deacetylation degree of 30 – 60 % which comprises the steps of :

35 a) filtrating a chitosan having a molecular weight of not smaller than 200 kDa and a deacetylation degree of 80 to 90 % dissolved in an acidic medium to eliminate insoluble particles;

b) precipitating chitosan contained in the filtrated acidic solution obtained in step a) to obtain chitosan free of insoluble particles;

c) preparing a cooled acidic solution of the chitosan free of insoluble particles obtained in step b) at a temperature lower than 5°C to obtain a cooled acidic solution of chitosan free of insoluble particles;

5 d) preparing a cooled acetic anhydride solution containing a predetermined amount of acetic anhydride in methanol at a temperature lower than 5°C;

e) reacetylating chitosan by adding dropwise, under homogeneous conditions, the cooled acetic anhydride solution of step d) to the cooled solution of chitosan prepared in step c) to provide a crude homogeneously reacetylated chitosan having a deacetylation degree of 30 – 60 %;

10 f) treating said crude chitosan obtained in step e) to eliminate salts produced during reacetylation and insoluble particles of chitosan to obtain a homogeneously reacetylated chitosan having a deacetylation degree of 30 – 60 %.

15 8. The process according to claim 7, wherein the treating step f) includes the steps of :

f-1) dialyzing chitosan obtained in step e) to eliminate salts produced during reacetylation in order to obtain a homogeneously reacetylated chitosan solution;

20 f-2) filtrating the chitosan solution obtained in step f-1) to eliminate insoluble particles of chitosan;

f-3) precipitating chitosan contained in the filtrated solution obtained in step f-2) and then drying chitosan to obtain a homogeneously reacetylated chitosan having a deacetylation degree of 30 – 60 %.

25 9. The process according to claim 8, wherein the precipitating step f-3) includes addition of a mixture of NH₄OH/methanol.

30 10. A homogeneously reacetylated chitosan having a molecular weight of not smaller than 200 kDa and a deacetylation degree of 30 – 60 % obtained by the process as claimed in anyone of claims 7-9 for use in the preparation of a pseudo-thermosetting neutralized chitosan composition forming a phosphate-free transparent hydrogel at a temperature higher than 5°C.

35 11. A process for producing a pseudo-thermosetting neutralized chitosan composition forming a phosphate-free, transparent hydrogel at a temperature higher than 5°C, which comprises the steps of :

g) solubilizing a homogeneously reacetylated chitosan derived from a chitosan having a deacetylation degree of 80 - 90 %, having a molecular weight of not smaller than 200 kDa and a deacetylation degree of 30 - 60 %, in an aqueous HCl medium and cooling said acidic chitosan solution at a temperature lower than 5 °C;

h) neutralizing the cooled chitosan solution obtained in step g) by adding an aqueous hydroxylated base previously cooled at a temperature lower than 5 °C to the cooled chitosan solution until the cooled solution of chitosan exhibits a pH of 6.8-7.2;

i) optionally, increasing the temperature of the neutral cooled solution of chitosan obtained in step h) at a temperature higher than 5 °C in order to induce pseudo-thermogelation.

12. The process according to claim 11, further comprising a step of sterilizing chitosan before the step g) of solubilization.

13. The process according to claim 11 or 12, wherein in step h), the hydroxylated base is NaOH.

14. The process according to anyone of claims 11 to 13, further comprising the step of adding an appropriate amount of a diol having a distance of at least 4.7 Å between the hydroxyl groups before, during or after the solubilization step g), or before, during or after the neutralization step h) to increase the consistency of the hydrogel to the required degree of consistency of the hydrogel.

15. The process according to claim 14, wherein the diol is 1,3-propanediol.

16. The process according to anyone of claims 11 to 15, wherein the homogeneously reacetylated chitosan solubilized in step g) is obtained by the process according to claims 7-9.

17. A phosphate-free transparent pseudo-thermosetting chitosan hydrogel obtained by the process as claimed in anyone of claims 11 to 16.

18. A use of a homogeneously reacetylated chitosan having a deacetylation degree of 30 – 60 % and a molecular weight of not smaller than 200 kDa obtained

by the process as claimed in anyone of claims 7 to 10, for the preparation of a phosphate-free, transparent, pseudo-thermosetting chitosan hydrogel.

19. A use of a pseudo-thermosetting neutralized chitosan composition as
5 claimed in anyone of claims 1-6, as a drug delivery system.